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Dr. C. W. Jameson
National Toxicology Program
Report on Carcinogens
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Dear Dr. Jameson:

Philip Morris takes this opportunity to respond to the call for final public comment on the possible listing of Environmental Tobacco Smoke (ETS) in the Report on Carcinogens, Ninth Edition, as noticed in 63 *Fed. Reg.* 68783, December 14, 1998. We provide in these comments i) a review of the Draft Background Document for Environmental Tobacco Smoke, ii) a comparison between the Draft Background Document for ETS with the Draft Background Document for Diesel Exhaust, and iii) an examination of claims made by Mr. James Repace at the December 2, 1998, meeting of the NTP's Board of Scientific Counselors Report on Carcinogens subcommittee.

In our review of the Draft Background Document for ETS we identify a number of inaccuracies and omissions. Of concern is the omission of a large body of published literature on human exposure to ETS by K. Phillips and co-workers, and the IARC multi-center study described by Boffetta et al., in the Journal of the National Cancer Institute (90(19), October 7, 1998). We also address inconsistencies in the Draft Background Document discussion of various ETS components in our review. We question in some detail the considerable emphasis placed by the Draft Background Document on the 1992 US EPA report, which has been vacated in a judicial proceeding. We review data suggesting that a considerable reduction in relative risk is obtained by correction for several sources of potential systematic bias in the relevant epidemiological studies. We also note that many of the animal studies reviewed in the Draft Background Document did not adhere to Good Toxicological Practices, because they used inappropriate test material and an inappropriate experimental animal, the A/J mouse, which NTP had previously rejected (1986) for use in carcinogenicity testing. With respect to the application of the Bradford Hill guidelines to the epidemiological data, our review of the complete data set on reported ETS exposure and lung cancer demonstrates that the data are inconsistent, represent an extremely weak association, and are of questionable biological plausibility, due to low exposure levels of individual components.

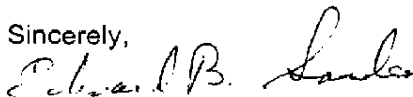
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We also submit a brief comparison of the Draft Background Document for ETS with the Draft Background Document for Diesel Exhaust, focusing on inconsistent treatment of the epidemiological data on these two substances, and how that treatment may have influenced the recent review by the RoC subcommittee. For instance, fourteen epidemiological studies of diesel exhaust were cited in the Draft Background Document for Diesel Exhaust, and the strengths and weaknesses each of the studies were reviewed. However, only four relevant studies (at least 30 have been published) were mentioned in the analogous section of the Draft Background Document for ETS, and no mention was made of any weaknesses in those studies. Also, in the Conclusions of the two Draft Background Documents, the authors make very different interpretations of very similar data.

In the last section of our submission, we review the relative risks derived by Mr. James Repace in both his written submission and public comments made on December 2. We demonstrate that Mr. Repace's theoretical models cannot, contrary to his statements, be verified by comparison to existing experimental data, and his suggestion that they can be is based on inappropriate assumptions regarding certain parameters in his models.

We believe that this commentary will be of value to your reviewers in their technical deliberations.

Sincerely,



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